

CLAIMS

1. A pharmaceutical composition for the treatment of IL-6 related diseases, comprising an interleukin 6 antagonist (IL-6 antagonist) and immunosuppressants.
- 5 2. A pharmaceutical composition comprising immunosuppressants, for effect enhancement on the use of IL-6 antagonist for the treatment of IL-6 related diseases.
- 10 3. A pharmaceutical composition comprising immunosuppressants, for the reduction or prevention of allergic reactions upon the treatment of IL-6 related diseases with an IL-6 antagonist.
4. A therapeutic agent for the administration at high doses, comprising an IL-6 antagonist.
- 15 5. A pharmaceutical composition comprising a high dose of IL-6 antagonist, for the reduction or prevention of allergic reactions upon the treatment of IL-6 related diseases.
- 20 6. The pharmaceutical composition according to any one of claims 1 to 5, wherein said IL-6 antagonist is an anti-interleukin-6 receptor antibody (IL-6R antibody).
7. The pharmaceutical composition according to claim 6, wherein said IL-6R antibody is a monoclonal antibody against IL-6R.
- 25 8. The pharmaceutical composition according to claim 6 or 7, wherein said anti-IL-6R antibody is a monoclonal antibody against human IL-6R.
9. The pharmaceutical composition according to claim 6 or 7, wherein said anti-IL-6R antibody is a monoclonal antibody against mouse IL-6R.
- 30 10. The pharmaceutical composition according to any one of claims 6 to 9, wherein said anti-IL-6R antibody is a recombinant antibody.
11. The pharmaceutical composition according to claim 8, wherein said human anti-IL-6R monoclonal antibody is PM-1 antibody.
- 35 12. The pharmaceutical composition according to

claim 9, wherein said mouse IL-6R monoclonal antibody is MR16-1 antibody.

13. The pharmaceutical composition according to any one of claims 6 to 12, wherein said anti-IL-6R antibody
5 is a chimera antibody, a humanized antibody or a human type antibody against IL-6R.

14. The pharmaceutical composition according to claim 13, wherein said humanized antibody against IL-6R is humanized PM-1 antibody.

15. The pharmaceutical composition according to any one of claims 1 to 14, wherein said IL-6 related diseases are rheumatoid arthritis, plasmacytosis,
10 hyperimmunoglobulinemia, anemia, nephritis, cachexia, multiple myeloma, Castleman's disease, mesangial proliferative nephritis, systemic lupus erythematosus,
15 Crohn's disease, ulcerative colitis, pancreatitis, psoriasis, juvenile idiopathic arthritis or systematic juvenile idiopathic arthritis, vasculitis and Kawasaki disease.

20 16. The pharmaceutical composition according to any one of claims 1 to 3 and claims 6 to 15, which is said pharmaceutical composition comprising the immunosuppressant or said pharmaceutical composition
25 comprising the antibody and the immunosuppressant, wherein a dosage of anti-IL-6R antibody is from 0.02 to 150 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

30 17. The pharmaceutical composition according to claim 16, wherein the dosage of anti-IL-6R antibody is from 0.5 to 30 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

35 18. The pharmaceutical composition according to claim 17, wherein the dosage of anti-IL-6R antibody is from 2 to 8 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

19. The pharmaceutical composition according to any

one of claims 4 to 15, which is said therapeutic agent for the treatment of IL-6 related diseases for the administration at high doses, comprising the anti-IL-6R antibody or said pharmaceutical composition comprising high doses of the anti-IL-6R antibody, wherein the dosage of anti-IL-6R antibody is 4 mg/kg/4 weeks or more or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

20. The pharmaceutical composition according to claim 19, wherein the dosage of anti-IL-6R antibody is from 6 to 16 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

21. The pharmaceutical composition according to claim 20, wherein the dosage of anti-IL-6R antibody is from 6 to 10 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

22. The pharmaceutical composition according to any one of claims 1 to 3 and claims 6 to 21, wherein said immunosuppressant is methotrexate (MTX).

23. The pharmaceutical composition according to claim 22, wherein the dosage of said MTX is from 1 to 100 mg/body/week.

24. The pharmaceutical composition according to claim 23, wherein the dosage of said MTX is from 4 to 50 mg/body/week.

25. The pharmaceutical composition according to claim 24, wherein the dosage of said MTX is from 7.5 to 25 mg/body/week.

26. The pharmaceutical composition according to any one of claims 1 to 3 and claims 6 to 25, for simultaneously administering said anti-IL-6 antibody and said immunosuppressant.

27. The pharmaceutical composition according to any one of claims 1 to 3 and claims 6 to 25, for administering said anti-IL-6 antibody and said immunosuppressant with time interval.

28. A use of an interleukin-6 antagonist (IL-6

antagonist) and immunosuppressants for the production of a pharmaceutical composition for the treatment of IL-6 related diseases.

5 29. A use of an IL-6 antagonist for the production of a pharmaceutical composition comprising immunosuppressants, for the effect enhancement on the use of the IL-6 antagonist for the treatment of IL-6 related diseases.

10 30. A use of an IL-6 antagonist for the production of a pharmaceutical composition comprising immunosuppressants, for the reduction or prevention of allergic reactions upon the treatment of IL-6 related diseases with the IL-6 antagonist.

15 31. A use of an IL-6 antagonist for the production of a therapeutic agent of IL-6 related diseases for the administration at high doses, comprising the IL-6 antagonist.

20 32. A use of an IL-6 antagonist for the production of a pharmaceutical composition comprising anti-IL-6R antibody at high doses for reduction or prevention of allergic reactions upon the treatment of IL-6 related diseases.

25 33. The use according to any one of claims 28 to 32, wherein said IL-6 antagonist is an anti-interleukin-6 receptor antibody (IL-6R antibody).

34. The use according to any one of claims 28 to 33, wherein said IL-6R antibody is a monoclonal antibody against IL-6R.

30 35. The use according to any one of claims 28 to 34, wherein said anti-IL-6R antibody is a monoclonal antibody against human IL-6R.

36. The use according to any one of claims 28 to 34, wherein said anti-IL-6R antibody is a monoclonal antibody against mouse IL-6R.

35 37. The use according to any one of claims 28 to 36, wherein said anti-IL-6R antibody is a recombinant antibody.

38. The use according to claim 35, wherein said human anti-IL-6R monoclonal antibody is PM-1 antibody.

39. The use according to claim 36, wherein said mouse anti-IL-6R monoclonal antibody is MR16-1 antibody.

5 40. The use according to any one of claims 32 to 39, wherein said anti-IL-6R antibody is a chimera antibody, a humanized antibody or a human type antibody against IL-6R.

10 41. The use according to claim 40, wherein said humanized antibody against IL-6R is humanized PM-1 antibody.

15 42. The use according to any one of claims 21 to 41, wherein said IL-6 related diseases are rheumatoid arthritis, plasmacytosis, hyperimmunoglobulinemia, anemia, nephritis, cachexia, multiple myeloma, Castleman's disease, mesangial proliferative nephritis, systemic lupus erythematosus, Crohn's disease, pancreatitis, psoriasis, juvenile idiopathic arthritis or systematic juvenile idiopathic arthritis.

20 43. The use according to any one of claims 28 to 30 and claims 33 to 42, which is said use for the production of the pharmaceutical composition comprising the immunosuppressant or the pharmaceutical composition comprising anti-IL-6 antibody and the immunosuppressant, 25 wherein a dosage of anti-IL-6R antibody is from 0.02 to 150 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

30 44. The use according to claim 43, wherein the dosage of anti-IL-6R antibody is from 0.5 to 30 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

35 45. The use according to claim 44, wherein the dosage of anti-IL-6R antibody is from 2 to 8 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

46. The use according to any one of claims 31 to 45, which is said use for the production of therapeutic

agent for the treatment of IL-6 related diseases for the administration at high dose, comprising the anti-IL-6R antibody or said pharmaceutical composition comprising high doses of the anti-IL-6R antibody, wherein the dosage of anti-IL-6R antibody is 4 mg/kg/4 weeks or more or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

47. The use according to claim 46, wherein the dosage of anti-IL-6R antibody is from 6 to 16 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

48. The use according to claim 47, wherein the dosage of anti-IL-6R antibody is from 6 to 10 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

49. The use according to any one of claims 28 to 30 and claims 33 to 48, wherein said immunosuppressant is methotrexate (MTX).

50. The pharmaceutical composition according to claim 49, wherein the dosage of said MTX is from 1 to 100 mg/body/week.

51. The pharmaceutical composition according to claim 50, wherein the dosage of said MTX is from 4 to 50 mg/body/week.

52. The pharmaceutical composition according to claim 51, wherein the dosage of said MTX is from 7.5 to 25 mg/body/week.

53. The use according to any one of claims 28 to 30 and claims 34 to 52, for simultaneously administering said anti-IL-6 antibody and said immunosuppressant.

54. The use according to any one of claims 28 to 30 and claims 34 to 52, for administering said anti-IL-6 antibody and said immunosuppressant with time interval.

55. A method comprising administering an IL-6 antagonist and immunosuppressants to a patient requiring such a treatment in the method for the treatment of IL-6 related diseases.

56. A method for the effect enhancement on the use of an IL-6 antagonist for the treatment of IL-6 related diseases, comprising administering immunosuppressants and an IL-6 antagonist to a patient requiring such a treatment.

57. A method for the reduction or prevention of allergic reactions upon the treatment of IL-6 related diseases with an IL-6 antagonist, comprising administering immunosuppressants and an IL-6 antagonist to a patient requiring such a treatment.

58. A method comprising administering an IL-6 antagonist anti-IL-6R antibody at a high dose to a patient requiring such a treatment in the method for the treatment of IL-6 related diseases with a high dose administration of an IL-6- antagonist.

59. A method for the reduction or prevention of allergic reaction upon the treatment of IL-6 related diseases, comprising administering a high dose administration of an IL-6 antagonist to a patient requiring such a treatment.

60. The method according to any one of claims 55 to 59, wherein said IL-6 antagonist is an anti-IL-6R antibody.

61. The method according to any one of claims 55 to 59, wherein said anti-IL-6R antibody is a monoclonal antibody against human IL-6R.

62. The method according to any one of claims 55 to 59, wherein said anti-IL-6R antibody is a monoclonal antibody against mouse IL-6R.

63. The method according to any one of claims 55 to 62, wherein said anti-IL-6R antibody is a recombinant antibody.

64. The method according to claim 61, wherein said human anti-IL-6R monoclonal antibody is PM-1 antibody.

65. The method according to claim 62, wherein said mouse anti-IL-6R monoclonal antibody is MR16-1 antibody.

66. The method according to any one of claims 59 to

64, wherein said anti-IL-6R antibody is a chimera antibody, a humanized antibody or a human type antibody against IL-6R.

5 67. The method according to claim 66, wherein said humanized antibody against IL-6R is humanized PM-1 antibody.

10 68. The method according to any one of claims 55 to 67, wherein said IL-6 related diseases are rheumatoid arthritis, plasmacytosis, hyperimmunoglobulinemia, anemia, nephritis, cachexia, multiple myeloma, Castleman's disease, mesangial proliferative nephritis, systemic lupus erythematosus, Crohn's disease, pancreatitis, psoriasis, juvenile idiopathic arthritis, or systematic juvenile idiopathic arthritis.

15 69. The method according to any one of claims 55 to 57 and claims 60 to 68, which is said method for the treatment wherein the immunosuppressant, or anti-IL-6R antibody and the immunosuppressant are administered, wherein a dosage of anti-IL-6R antibody is from 0.02 to 20 150 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

25 70. The method according to claim 69, wherein the dosage of anti-IL-6R antibody is from 0.5 to 30 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

 71. The method according to claim 70, wherein the dosage of anti-IL-6R antibody is from 2 to 8 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

30 72. The method according to any one of claims 58 to 68, which is said method for the treatment of IL-6 related diseases or said method for the treatment wherein a high dose of anti-IL-6R antibody is administered comprising administering the high dose of anti-IL-6R 35 antibody, wherein the dosage of anti-IL-6R antibody is 4 mg/kg/4 weeks or more or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

73. The method according to claim 72, wherein the dosage of anti-IL-6R antibody is from 6 to 16 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

5 74. The method according to claim 73, wherein the dosage of anti-IL-6R antibody is from 6 to 10 mg/kg/4 weeks or the dosage showing an anti-IL-6R antibody concentration in blood equivalent thereto.

10 75. The method according to any one of claims 55 to 57 and claims 60 to 74, wherein said immunosuppressant is methotrexate (MTX).

76. The method according to claim 75, wherein the dosage of said MTX is from 1 to 100 mg/body/week.

15 77. The method according to claim 76, wherein the dosage of said MTX is from 4 to 50 mg/body/week.

78. The method according to claim 77, wherein the dosage of said MTX is from 7.5 to 25 mg/body/week.

20 79. The method according to any one of claims 55 to 57 and claims 60 to 78, for simultaneously administering said anti-IL-6R antibody and said immunosuppressant.

80. The use according to any one of claims 55 to 57 and claims 60 to 78, for administering said anti-IL-6R antibody and said immunosuppressant with time interval.